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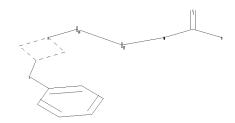
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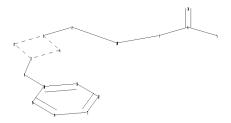
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chain bonds :
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ring bonds :
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exact/norm bonds :
1-2  1-6  1-8  3-4  3-20  4-5  4-16  6-7  7-8  7-9  9-10
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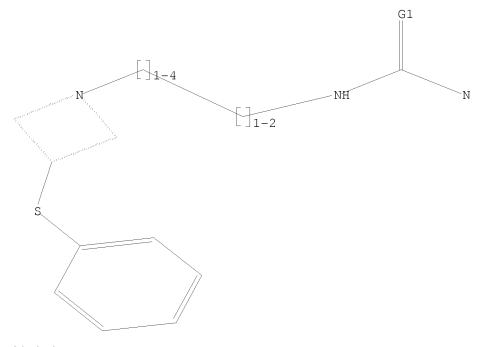
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TITLE: Preparation of 1,3-disubstituted azetidine

derivatives for use as CCR-3 receptor antagonists in the

treatment

of inflammatory and allergic diseases Le Grand, Darren Mark Novartis Ag, Switz.; Novartis Pharma GmbH PCT Int. Appl., 84 pp. CODEN: PIXXD2 Patent INVENTOR(S):
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|  |  |   |                        |                            |  |                   |  | APPLICATION NO.  |                   |  |  |  |   |                   |   |  |   |
|--|--|---|------------------------|----------------------------|--|-------------------|--|--|-------------------|--|--|--|---|-------------------|---|--|---|
|  |  |   |                        |                            |  |                   |  |  | WO 2004-EP10260   |  |  |  |   |                   |   |  |   |
|  | W:   | CN,<br>GE,  | CO,<br>GH,             | CR,<br>GM,                 | CU,<br>HR,                                     | CZ,<br>HU,        | DE,  | DK,<br>IL,   | DM,<br>IN,        | DZ<br>IS                                     | B, BG,<br>E, EC,<br>B, JP,<br>G, MK,                         | EE,<br>KE,   | EG,<br>KG,                              | ES,<br>KP,        | FI,<br>KR,                                | GB,<br>KZ,   | GD,<br>LC,                                    |
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|  |  | EE,<br>SI,  | ES,                    | FI,<br>TR,                 | FR,  | GB,               | GR,  | HU,  | IE,               | II   | r, BE.<br>r, LU.<br>1, GA.                                   | MC,  | NL,                                     | PL,               | PT,                                       | RO,  | SE,   |
|  |  |   |                        |                            |  |                   |  | AU 2004-272275   |                   |  |  | 20040914   |   |                   |   |  |   |
| CA<br>EP                                     |  |   |                        | A1 20050324<br>A1 20060607 |  |                   |  | CA 2004-2534550<br>EP 2004-765174                                  |                   |  |  |  |   |                   |   |  |   |
| CN<br>BR<br>JP<br>AT<br>PT<br>ES<br>MX<br>US | R:<br>1849<br>2004<br>2007<br>3651<br>1663<br>2286 | AT,<br>IE,<br>302<br>0144:<br>5050:<br>55<br>966<br>664<br>0028 | BE,<br>SI,<br>16<br>80 | CH,<br>FI,                 | DE,<br>RO,<br>A<br>A<br>T<br>T<br>E<br>T3<br>A | DK,<br>CY,        | ES,<br>TR,<br>2006<br>2006<br>2007<br>2007<br>2007<br>2007<br>2006 | FR,<br>BG,<br>1018<br>1114<br>0308<br>0715<br>0926<br>1201<br>0605 | CZ,               | CN<br>BR<br>JP<br>AT<br>PT<br>ES<br>MX<br>US | 2004<br>2004<br>2004<br>2004<br>2004<br>2004<br>2004<br>2004 | PL,<br>-8002<br>-1441<br>-5257<br>-7651<br>-7651<br>-2870<br>-5684 | SK<br>6204<br>6<br>89<br>74<br>74<br>74 | ŕ                 | 2<br>2<br>2<br>2<br>2<br>2<br>2<br>2<br>2 | 0040<br>0040<br>0040<br>0040<br>0040<br>0040<br>0060 | 914<br>914<br>914<br>914<br>914<br>914<br>314 |
|  |  |   |                        |                            |  |                   |  |  |                   |  | 2003   |  |   |                   |   |  |   |
|  |  |   |                        |                            |  |                   |  |  |                   | WO   | 2004   | EP10   | 260                                     | 1                 | W 2                                       | 0040   | 914   |

CASREACT 142:336234; MARPAT 142:336234

(Continued)

ANSWER 1 OF 1 CAPLUS COPYRIGHT 2010 ACS on STN Absolute stereochemistry

OTHER SOURCE(S):

 $848642-40-0 \quad \text{CAPLUS} \\ \text{Urea, N-[(1S)-3-[3-[(4-\text{chlorophenyl})sulfinyl]-1-azetidinyl]-1-(hydroxymethyl)propyl]-N'-(5-\text{ethyl-1,3,4-thiadiazol-2-yl})- \quad (CA \text{ INDEX } ) \\ \text{(CAPLUS } \\ \text{(CAPLUS } ) \\ \text{(CAPLUS } )$ 

Absolute stereochemistry.

848642-41-1 CAPLUS
Urea, N-[(1S)-3-[3-[(4-chlorophenyl)sulfinyl]-1-azetidinyl]-1-(hydroxymethyl)propyl]-N'-(3-ethyl-1-methyl-1H-pyrazol-5-yl)NAME) (CA INDEX

Absolute stereochemistry.

848642-42-2 CAPLUS

ANSWER 1 OF 1 CAPLUS COPYRIGHT 2010 ACS on STN (Continued)

AB Compds. of formula I and II [Ar = Ph optionally substituted by one or more  $\frac{1}{2}$ 

substituents selected from halo, C1-C8-alkyl, cyano, nitro; X1 = S, S(O), S(O)2; X2 = C(O), O, CH2, S, S(O), S(O)2; m = 1, 2, 3, 4; R1 = B, C1-C8-alkyl optionally substituted; Q = C(Rb) (Rc) where Rb and Rc are independently C1-C8-alkyl or Rb and Rc together form a C3-C10-cycloalkyl; Y = O, S; R2 = H, C1-C8-alkyl, C3-C10-cycloalkyl; R3 = C1-C8-alkyl c3-C10-cycloalkyl; R3 = C1-C8-alkyl optionally having a benzo group, a heterocyclic group] were prepared and

useful for treating a banc group, a neterocyctra group, act prepared and useful for treating conditions that are mediated by CCR-3, for example an inflammatory or allergic condition, particularly an inflammatory or obstructive airways disease. E.g., 1-benzhydryl-3-(4-chlorophenylsulfanyl) azetidine was oxidized with MCPBA, and treated with 1-chloroethoxycarbonyl chloride to give 3-(4-chlorobenzenesulfinyl) azetidine. Reaction of the latter with [(S)-1-(tert-butyldiphenylsilanyloxymethyl)-3-iodopropyl] carbamic acid tert-Bu ester gave [(S)-1-(tert-butyldiphenylsilanyloxymethyl)-3-[3-(4-chlorophenylsulfinyl) azetidin-1-y1]propyl]carbamic acid tert-Bu ester. The latter was desilylated, then treated with TTA to give (S)-2-amino-4-[3-(4-chlorophenzensulfinyl) azetidin-1-y1]butan-1-ol. Reaction of the latter with 3,5-dimethoxyphenyl isocyanate resulted in

1-[(S)-3-[3-(4-chlorobenzenesulfinyl)azetidin-1-yl]-1-hydroxymethylpropyl]-

(Uses)
(preparation of 1,3-disubstituted azetidine derivs. for use as CCR-3 receptor antagonists in the treatment of inflammatory and allergic diseases)
888642-39-7 CAPLUS
(Usea, N-[(18)-3-[3-[(4-chlorophenyl)sulfinyl]-1-azetidinyl]-1-(hydroxymethyl)propyl]-N'-(3,5-dimethoxyphenyl)- (CA INDEX NAME)

ANSWER 1 OF 1 CAPLUS COPYRIGHT 2010 ACS on STN (Continued)
Usea, N={(15)-3-[3-[(4-chlorophenyl)sulfinyl]-1-azetidinyl]-1-(hydroxymethyl)propyl]-N'-(3-cyclopropyl-1-methyl-1H-pyrarol-5-yl)- (CA
RUDEX NAME)

Absolute stereochemistry

848642-43-3 CAPLUS
Urea, N-[(18)-3-[3-[(4-chloropheny1)sulfiny1]-1-azetidiny1]-1-(hydroxymethy1)propy1]-N'-(5-ethy1-3-isoxazoly1)- (CA INDEX NAME)

Absolute stereochemistry.

848642-44-4 CAPLUS
Urea, N-[(1S)-3-[3-[(4-chlorophenyl)sulfinyl]-1-azetidinyl]-1-(hydroxymethyl)propyl]-N'-(3-ethyl-5-isoxazolyl)- (CA INDEX N

Absolute stereochemistry.

L6 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2010 ACS on STN Absolute stereochemistry. (Continued)

848642-46-6 CAPLUS
Urea, N-[(1S)-3-[3-[(4-chlorophenyl)sulfinyl]-1-azetidinyl]-1(methoxymethyl)propyl]-N'-(5-ethyl-1,3,4-thiadiazol-2-yl)- (CA INDEX NAME)

Absolute stereochemistry.

848642-47-7 CAPLUS

Urea, N=[(1S)-3-[3-[(4-chlorophenyl)sulfinyl]-1-azetidinyl]-1(methoxymethyl)propyl]-N'-(3-ethyl-1-methyl-1H-pyrazol-5-yl)- (CA INDEX CN

Absolute stereochemistry.

848642-48-8 CAPLUS Urea, N-[(1S)-3-[3-[(4-chlorophenyl)sulfinyl]-1-azetidinyl]-1-

ANSWER 1 OF 1 CAPLUS COPYRIGHT 2010 ACS on STN (Continued)

848642-52-4 CAPLUS Urea, N-[(1R)-3-[3-[(4-chloropheny1)sulfiny1]-1-azetidiny1]-1-methylproy1]-N'-(5-ethy1-1,3,4-thiadiazo1-2-y1)- (CA INDEX NAME)

Absolute stereochemistry.

848642-53-5 CAPLUS Urea, N-[(1R)-3-[3-[(4-chlorophenyl)sulfinyl]-1-azetidinyl]-1-methylpropyl]-N'-(3-ethyl-1-methyl-1H-pyrazol-5-yl)- (CA INDEX NAME)

Absolute stereochemistry.

 $848642-54-6 \quad CAPLUS \\ Uzea, N-[(1R)-3-[3-[(4-chlorophenyl)sulfinyl]-1-azetidinyl]-1-methylpropyl]-N'-(3-cyclopropyl-1-methyl-1H-pyrazol-5-yl)- (CA INDEX NAME)$ 

ANSWER 1 OF 1 CAPLUS COPYRIGHT 2010 ACS on STN (Continued) (methoxymethyl)propyl]-N'-(3-cyclopropyl-1-methyl-1H-pyrazol-5-yl)- (CA INDEX NAME)

Absolute stereochemistry.

Absolute stereochemistry.

848642-50-2 CAPLUS Urea, N-[(18)-3-[3-[(4-chlorophenyl)sulfinyl]-1-azetidinyl]-1-(methoxymethyl)propyl]-N'-(3-ethyl-5-isoxazolyl)- (CA INDEX NAME)

Absolute stereochemistry.

Absolute stereochemistry.

L6 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2010 ACS on STN Absolute stereochemistry. (Continued)

Absolute stereochemistry.

848642-56-8 CAPLUS
Urea, N-[(1R)-3-[3-[(4-chlorophenyl)sulfinyl]-1-azetidinyl]-1-methylpropyl]-N'-(3-ethyl-5-isoxazolyl)- (CA INDEX NAME)

Absolute stereochemistry.

848642-57-9 CAPLUS
Urea, N-[(1S)-3-[3-[(4-chlorophenyl)thio]-1-azetidinyl]-1(hydroxymethyl)propyl]-N'-(5-ethyl-1,3,4-thiadiazol-2-yl)- (CA INDEX NAME)

Absolute stereochemistry.

 $848642-58-0 \quad CAPLUS \\ Urea, N-[(1S)-3-[3-[(4-chloropheny1)thio]-1-azetidiny1]-1-((hydroxymethy1)propy1]-N'-(3-ethy1-1-methy1-1H-pyrazo1-5-y1)- (CA INDEX NAME)$ 

Absolute stereochemistry.

848642-59-1 CAPLUS

Urea, N-[(1S)-3-[3-[(4-chlorophenyl)thio]-1-azetidinyl]-1(hydroxymethyl)propyl]-N'-(3-cyclopropyl-1-methyl-1H-pyrazol-5-yl)- (CA
INDEX NAME)

Absolute stereochemistry.

848642-60-4 CAPLUS
Urea, N=[(1S)-3-[3-[(4-chlorophenyl)thio]-1-azetidinyl]-1(hydroxymethyl)propyl]-N'-(3,5-dimethoxyphenyl)- (CA INDEX NAME)

Absolute stereochemistry.

ANSWER 1 OF 1 CAPLUS COPYRIGHT 2010 ACS on STN (Continued)

 $848642-64-8 \quad CAPLUS \\ Uzea, N-[(15)-3-[3-[(4-chloropheny1)sulfony1]-1-azetidiny1]-1-(hydroxymethy1)propy1]-N'-(3-ethy1-1-methy1-1H-pyrazo1-5-y1)- (CA INDEX NAME)$ 

Absolute stereochemistry.

 $848642-65-9 \quad CAPLUS \\ Urea, \ N-[(1S)-3-[3-[(4-chlorophenyl)sulfonyl]-1-azetidinyl]-1-(hydroxymethyl)propyl]-N'-(3-cyclopropyl-1-methyl-1H-pyrazol-5-yl)- (CA INDEX NAME)$ 

Absolute stereochemistry.

848642-66-0 CAPLUS
Urea, N-[(18)-3-[3-[(4-chlorophenyl)sulfonyl]-1-azetidinyl]-1-(hydroxymethyl)propyl]-N'-(3,5-dimethoxyphenyl)- (CA INDEX NAME)

Absolute stereochemistry.

L6 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2010 ACS on STN (Continued)

848642-61-5 CAPLUS
Urea, N-[(1S)-3-[3-[(4-chlorophenyl)thio]-1-azetidinyl]-1(hydroxymethyl)propyl]-N'-(5-ethyl-3-isoxazolyl)- (CA INDEX NAME)

Absolute stereochemistry.

848642-62-6 CAPLUS
Usea, N-[(1S)-3-[3-[(4-chlorophenyl)thio]-1-azetidinyl]-1(Nydroxymethyl)propyl]-N'-(3-ethyl-5-isoxazolyl)- (CA INDEX NAME)

Absolute stereochemistry.

848642-63-7 CAPLUS
Urea, N-[(1S)-3-[3-[(4-chlorophenyl)sulfonyl]-1-azetidinyl]-1(hydroxymethyl)propyl]-N'-(5-ethyl-1,3,4-thiadiazol-2-yl)- (CA INDEX

Absolute stereochemistry.

L6 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2010 ACS on STN (Continued)

848642-67-1 CAPLUS
Uzea, N-[(1S)-3-[3-[(4-chloropheny1)sulfony1]-1-azetidiny1]-1-(hydroxymethy1)propy1]-N'-(5-ethy1-3-isoxazoly1)- (CA INDEX NAME)

Absolute stereochemistry.

848642-68-2 CAPLUS Urea, N-[(1S)-3-[3-[(4-chlorophenyl)sulfonyl]-1-azetidinyl]-1- (hydroxymethyl)propyl]-N'-(3-ethyl-5-isoxazolyl)- (CA INDEX NAME)

Absolute stereochemistry.

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